Blood Volume in Cardiac Decompensation

Determinations by Use of Radiochromium

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• *Radiochromium has these advantages for the measurement of whole blood volume: it remains in the erythrocytes many hours; it can be measured easily and accurately; the amount of radiation from it is very low.*

As measured by the radiochromium method, the whole blood volume of normal patients was determined to be 65.6 cc. ± 5.95 cc. per kilogram of body weight or 2.49 ± 0.28 liters per square meter of body surface.

In a majority of a series of patients with heart disease, hypervolemia was found during right ventricular failure but not in those having left ventricular failure or mitral stenosis alone.

IN CONGESTIVE HEART FAILURE, the blood volume has been considered generally to be increased.[1, 2, 5, 6, 7] Recently Prentice and co-workers[9] and Ross and co-workers,[11] by tagging erythrocytes with P^{32} obtained evidence that the blood volume during heart failure is not always increased.

Nylin and Hedlund[8] in 1947 summarized the opinions of various investigators regarding the efficiency of various methods of determining the volume of blood. They concluded that the dye and carbon monoxide methods may result in falsely high values because of leakage of dye from the vascular system and because carbon monoxide leaves the erythrocytes and goes to myoglobin. More accurate determinations of blood volume probably can be made by using radioisotopes to tag erythrocytes.[3,4,5,7,9,12]

In the present study radiochromium was selected as the tagging material for the following reasons:[10] It passes into the erythrocytes in vitro if used in the sodium chromate form; it remains in the erythrocytes for 12 to 24 hours approximately at the original concentrations, permitting unhurried and accurate measurements; it emits mainly gamma rays which are detected efficiently by a scintillation counter; the radiation dosage to the subject is low and is not dangerous.

METHOD

Ten milliliters of heparinized blood was withdrawn into a sterile rubber-stoppered tube containing 10 to 15 microcuries of sodium chromate ($Na_2Cr^{51}O_4$ of high specific activity* carried by no more than 100 to 300 micrograms of inert chromium. The sample was gently agitated by a shaker for 45 minutes at room temperature to permit maximal uptake. This was 60 to 98 per cent of the Cr^{51} as $Na_2Cr^{51}O_4$ by the erythrocytes. The uptake is inversely proportional to the amount of carrier chromium present. The excess $Na_2Cr^{51}O_4$ and plasma was removed by washing and centrifuging (1559 gravities) the red cells three times with normal saline solution. The cells were resuspended to approximately the original volume by adding normal saline solution; an aliquot of 0.5 ml. of this cell-saline mixture was diluted to 50 ml. for a standard, used for determining the number of counts per ml. injected. The carefully noted volume remaining of the cell-saline mixture was injected intravenously into the patient.

In subjects with normal circulation, complete mixing of the injected material with the circulating blood required between 10 and 15 minutes but in some patients with cardiac disease 30 minutes was necessary. To be safe, samples (5 to 7 ml.) were taken for measurement 60 minutes after injection.

The blood volume, which is apparent and not truly total, was measured on the sample of whole blood, rather than the erythrocyte mass, in order to avoid the differences between the hematocrit of blood from large vessels and the hematocrit of all the blood in the body. Although it was not done, it would have been possible to compute the erythrocyte and plasma volumes by using the hematocrit values. The formula, employing the dilation of the tagged dose, was:

$$\text{Blood volume in cc.} = \frac{\text{Total counts per second of injected } Cr^{51}}{\text{Counts per second per cc. of blood withdrawn}}$$

The reliability of the method was tested by reinjecting each of 17 patients with a second larger

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*The sodium chromate[51] was obtained from either Oak Ridge National Laboratory or the Abbott Laboratories of North Chicago.

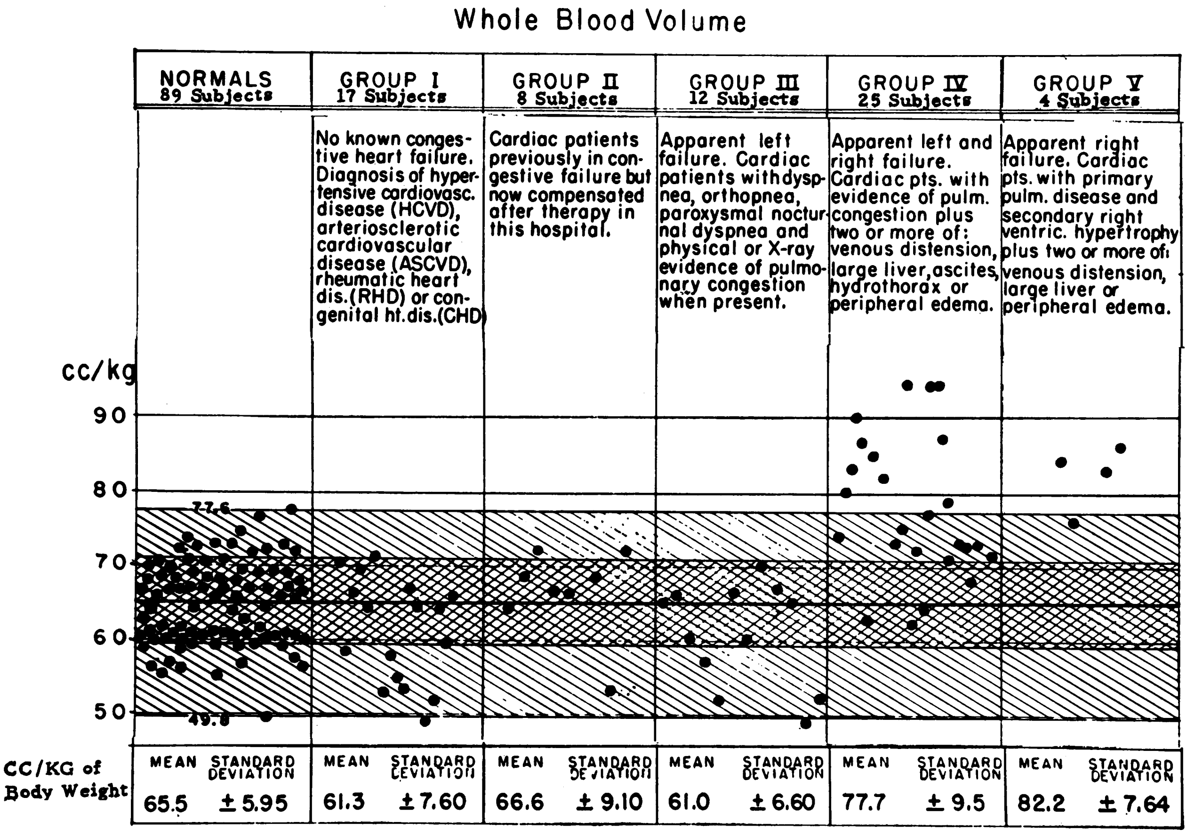

CHART 1

dose of Cr^{51} one hour after the first dose. The differences between the two computations of total volume ranged from as little as 30 cc. to as much as 540 cc. or from 0.4 per cent to 10 per cent.

CLINICAL TESTS

Normal values were determined on 89 adult males, mostly ambulatory, who were awaiting elective surgical repair of such conditions as hernia, varicose veins and hemorrhoids. None had conditions which conceivably might have disturbed the volume of blood. Fifty-six patients with cardiac disease were tested. They were divided into five groups (see Chart 1). Some patients were included in one group at one time and in a different group at the time of subsequent tests owing to changes in their status in the interim. Group I (17 patients) was made up of patients who never had had congestive heart failure; Group II (8 patients) of those who had had congestive failure but were in a compensated state at the time of the test; Group III (12 patients) those with left-sided failure manifested by pulmonary congestion; Group IV (25 patients) those with left and right ventricular failure; Group V (4 patients) those with primary pulmonary disease and right-sided failure.

RESULTS

Normal values were:

	Total cc.	cc. per kg. of body weight	Liters of blood per square meter of body area
Range	2500 - 6074	45.8 - 77.6	1.79 - 3.05
Mean ± standard deviation		65.5 ± 5.95	2.49 ± 0.28

In the patients with cardiac disease (see Chart 1), Group I, Group II, and Group III, the blood volumes were within the normal range; in Groups IV and V the majority had significantly elevated blood volumes. Statistical analysis showed data for Group I were highly significant (probability=0.01); Group II showed no significant difference from normal. Group III volumes were significantly lower than normal calculated as cubic centimeters per kilogram of body weight "wet"† (probability = 0.02) but almost the same when calculated at "dry" weight. Using liters of blood per square meter of body surface area, the volumes were below normal "wet" (probability = 0.03) but not significantly lower "dry" (probability = 0.3). Volumes of Group IV and V were significantly higher whether calculated as cubic centimeters per kilogram of body weight or L./Sq.M, "wet" or "dry" weight (probability = less than 0.01).

†"Dry weight" was the lowest weight reached after compensation was established.

DISCUSSION

Increased blood volumes occurred in the majority of persons having signs and symptoms of right ventricular failure, for example, venous engorgement, ascites and peripheral edema. In no case in which the patient had signs and symptoms of pulmonary congestion alone (due to left ventricular failure or mitral stenosis) was the blood volume elevated. However, there were five patients having the signs and symptoms of right ventricular failure who had blood volumes within the range of normal; when computed on "dry" weight only one of these was normal. The authors have no explanation for this finding.

Although not included with the results there were 16 patients who had serial blood volume studies during treatment for cardiac failure. As their peripheral edema, ascites and liver engorgement disappeared the blood volumes reverted toward normal values; the opposite was true in patients who became clinically worse. It was also noted that the increased volumes in patients with cor pulmonale reverted to the normal range as the signs and symptoms of right ventricular failure disappeared under therapy and that the total increases of the blood volume in these patients was not entirely due to secondary polycythemia.

The findings in the present study closely approximated those of Nylin and Hedlund[8] who also found hypervolemia most pronounced in patients with severe edema and slight in those with pulmonary congestion. In the present series the hypervolemia was roughly proportional to the amount of edema and excess body weight. Etiological factors (rheumatic heart disease, arteriosclerotic heart disease, hypertensive cardiovascular disease, etc.) had no apparent relation or effect on the blood volume in any given patient in any of the groups tested.

The chain of events in the evolution of cardiac failure has been a controversial subject. Probably the most generally accepted definition of cardiac failure is an insufficient output relative to the needs of the organism. Insufficient output of the left ventricle results in a relative state of anoxia; the organs such as the kidneys, liver and endocrine glands evoke reactions to retain salt and water. The exact hemodynamics in all the mechanisms is not known. Apparently at the stage of cardiac failure when only pulmonary congestion is present there is no hypervolemia, according to the results noted in the present study, even though these patients retain salt and water as shown by diuresis and weight loss following cardiac therapy. As Ross[11] pointed out, there may be a relative shift of the total blood volume to the pulmonary vascular bed without an overall blood volume increase in these patients with left ventricular failure alone. This may be explained by the relative unequality in the output of the two ventricles, the right ventricle ejecting more blood per beat than the left. Clinically, this theory has some support in that the pulmonary congestive signs and symptoms are relieved partially when the right ventricle fails. With the failure of the right ventricle there is the factor of less venous blood being passed to the pulmonary vascular bed with a greater volume of blood being pooled in the greater venous circulation. The authors feel that this venous pooling and congestion probably contributes greatly to the hypervolemia as well as to the hepatomegaly, ascites and peripheral edema. It is recognized that there are many factors that enter into the problem of cardiac failure and that this venous pooling may not be the main factor in any given patient.

By this method the whole blood volume of normal patients was determined to be 65.5 cc. $\pm$ 5.95 cc. per kilogram of body weight or 2.49 $\pm$ 0.28 liters per square meter of body surface. In a majority of a series of patients with heart disease hypervolemia was found during right ventricular failure but not in those having left ventricular failure or mitral stenosis alone.

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